

IN THE SPECIFICATION:

Please amend the specification as follows:

Delete the word "NOVEL" from the title of the specification, so that the title reads:  
"ARTEMIN, A NEUROTROPHIC FACTOR", and

In the table on page 64, at line 15, following the terms "December 22, 1998", add ---  
203,559 ---.

IN THE CLAIMS:

Please amend the claims as follows:

*Subj 1*  
12. (Twice amended) A [nucleic acid comprising a] polynucleotide encoding a pan-growth factor which polynucleotide comprises [comprising] a nucleotide sequence of not over about 10,000 nucleotides encoding an artemin amino acid sequence or a conservatively substituted variant thereof or a fragment thereof of at least 8 contiguous amino acids which nucleotide sequence is capable of specifically hybridizing to a nucleotide sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:60, SEQ ID NO:61 and SEQ ID NO:62, and which polynucleotide also comprises a nucleotide sequence encoding a fragment containing an active domain of at least one other growth factor from the TGF- $\beta$  superfamily.

*Subj 2*  
15. (Twice amended) An isolated and purified nucleic acid molecule or [nucleic acid molecule complementary thereto] fragment thereof wherein the isolated and purified nucleic acid molecule comprises [comprising] a nucleotide sequence encoding an artemin amino acid sequence or a conservatively substituted variant thereof, which nucleic acid molecule or fragment thereof contains from at least 15 to no more than about 10,000 nucleotides and is capable of specifically hybridizing to a nucleotide sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:60, SEQ ID NO:61 and SEQ ID NO:62. [or a fragment of said nucleotide sequence consisting of at least 15 contiguous nucleotides.]

16. (Amended) The isolated and purified nucleic acid molecule [or nucleic acid molecule complementary thereto] of claim 15, wherein the nucleic acid molecule comprises [comprising] a nucleotide sequence encoding an artemin polypeptide which promotes survival of trigeminal ganglion neurons, nodose ganglion neurons, superior cervical ganglion neurons, and tyrosine-hydroxylase-

*C20*  
expressing dopaminergic ventral midbrain neurons wherein said nucleic acid molecule specifically hybridizes to a [mature human artemin] nucleotide sequence encoding mature human artemin as set forth in SEQ ID NO:6, SEQ ID NO:7 or SEQ ID NO:8 or to a [mature mouse artemin] nucleotide sequence encoding mature mouse artemin as set forth in SEQ ID NO:37, SEQ ID NO:38 or SEQ ID NO:39, or to the complement of said sequence.

*C3*  
21. (Amended) The isolated and purified nucleic acid molecule of claim 15 comprising ATCC deposit number 203559 made on December 22, 1998.

*Ref G3*  
*C4*  
23. (Amended) The isolated and purified nucleic acid molecule of claim 15 comprising a polynucleotide encoding a polypeptide selected from the group consisting of a human pro-artemin as set forth in [SEQ ID NO:41] SEQ ID NO:40, a human pre-pro artemin as set forth in SEQ ID NO:26 or SEQ ID NO:32, a mouse pro-artemin as set forth in [SEQ ID NO:42] SEQ ID NO:41, a mouse pre-pro-artemin as set forth in SEQ ID NO:29 and a polypeptide comprising a non-artemin pre-pro- region sequence and a human or mouse mature artemin amino acid sequence.

*Ref D4*  
*C5*  
25. (Amended) A recombinant nucleic acid molecule comprising an artemin nucleotide sequence [or complement thereto] wherein the artemin nucleotide sequence encodes an amino acid sequence selected from the group consisting of a pre-pro-artemin polypeptide, a pro-artemin polypeptide, a mature artemin polypeptide, a conservatively substituted variant thereof and a fragment of said artemin amino acid sequence [thereof] having at least 8 contiguous amino acids, and wherein the artemin nucleotide sequence is capable of specifically hybridizing to a nucleotide sequence selected from the group consisting of SEQ ID NO:6, SEQ ID NO:7, SEQ ID NO:8, SEQ ID NO:9, SEQ ID NO:10, SEQ ID NO:11, SEQ ID NO:37, SEQ ID NO:38, SEQ ID NO:39, SEQ ID NO:60, SEQ ID NO:61 and SEQ ID NO:62.

26. (Amended) An [The isolated and purified polynucleotide of claim 15 which is an artemin] antisense oligonucleotide which is complementary to the nucleic acid molecule of claim 15.

*Ref D5*  
27. An isolated and purified nucleic acid molecule comprising a polynucleotide encoding:  
(a) a pre- region of artemin as set forth in SEQ ID NO:54 or SEQ ID NO:55;  
(b) a pro- region of artemin as set forth in SEQ ID NO:56 or SEQ ID NO:57;  
(c) a pre-pro- region of artemin as set forth in SEQ ID NO:58 or SEQ ID NO:59; or

(d) a conservatively substituted variant of (a), (b) or (c) wherein the polynucleotide encoding said conservatively substituted variant is capable of specifically hybridizing to a nucleic acid sequence selected from the group consisting of SEQ ID NO:24, SEQ ID NO:27, SEQ ID NO:30 and SEQ ID NO:46, or a complement thereof.

Please add the following new claims:

*Sur D6* 39. The nucleic acid comprising a polynucleotide encoding a pan-growth factor according to claim 12, wherein the at least one other growth factor from the TGF- $\beta$  superfamily is selected from the group consisting of transforming growth factor- $\beta$ 1 (TGF $\beta$ 1), transforming growth factor- $\beta$ 2 (TGF $\beta$ 2), transforming growth factor- $\beta$ 3 (TGF $\beta$ 3), inhibin  $\beta$  A (INH $\beta$ A), inhibin  $\beta$  B (INH $\beta$ B), the *nodal* gene (NODAL), bone morphogenetic proteins 2 and 4 (BMP2 and BMP4), the *Drosophila decapentaplegic* gene (*dpp*), bone morphogenetic proteins 5-8 (BMP5, BMP6, BMP7 and BMP8), the *Drosophila* 60A gene family (60A), bone morphogenetic protein 3 (BMP3), the *Vg1* gene, growth differentiation factors 1 and 3 (GDF1 and GDF3), dorsalin (drsln), inhibin  $\alpha$  (INH $\alpha$ ), the *MIS* gene (MIS), growth factor 9 (GDF-9), glial-derived neurotrophic growth factor (GDNF), neuritin (NTN) and persephin..

#### REMARKS

In the specification, the title of the application has been amended as suggested in the Action of May 18, 2000, by deleting the word "NOVEL". Also, the ATCC number of the plasmid deposited on December 22, 1998, has been added to the table on page 64. A copy of the ATCC International Form is attached hereto.

Claims 12, 15, 16, 21, 23, 25, 26 and 27 have been amended.

Claim 12 has been amended by limiting the size of the nucleotide sequence encoding artemin to not over about 10,000 nucleotides, support for which is found at least at page 30, lines 3 - 6 of the specification. Support for the nucleic acid sequences that have been added is found at least at page 7, lines 28 - 32. Support for the description of the inclusion of "an active domain" of the non-artemin TGF- $\beta$  family member is found at least at page 31, lines 20 - 24.

Claim 15 has been amended by clarifying that it is the nucleic acid (rather than both the nucleic acid and its complement) that is capable of specifically hybridizing with specific nucleotide sequences. Support for the group of nucleotide sequences is found at least at page 7, lines 28 - 32 of the specification. The claims has also been amended to describe the nucleotide as having from at least 15 to about 10,000 nucleotides. Support for the upper limit is found at least at page 30, lines 3 - 6 of the specification.